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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/020,393	02/09/98	SIMS F	UMAF-170

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EXAMINER	
GAMBEL, P	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 01/28/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

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09/020393

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EXAMINER

ART UNIT	PAPER NUMBER
	16

DATE MAILED:

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

OFFICE ACTION SUMMARY

☑ Responsive to communication(s) filed on 11/15/99

☑ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 D.C. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☑ Claim(s) 1-35 is/are pending in the application.
Of the above, claim(s) 1-9, 13-15, 18-35 is/are withdrawn from consideration.
☐ Claim(s) _____ is/are allowed.
☑ Claim(s) 10-12, 16, 17 is/are rejected.
☐ Claim(s) _____ is/are objected to.
☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
☐ The specification is objected to by the Examiner.
☐ The oath or declaration is objected to by the Examiner.

FORMAL DRAWINGS FILED 5/18/99, ARE ACCEPTABLE

Priority under 35 U.S.C. § 119

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.
☐ received in Application No. (Series Code/Serial Number) _____.
☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of Reference Cited, PTO-892
☑ Information Disclosure Statement(s), PTO-1449, Paper No(s). 13
☐ Interview Summary, PTO-413
☐ Notice of Draftperson's Patent Drawing Review, PTO-948
☐ Notice of Informal Patent Application, PTO-152

--SEE OFFICE ACTION ON THE FOLLOWING PAGES--

★ U.S. GPO: 1996-404-496/40517

DETAILED ACTION

1. Applicant's amendment, filed 11/15/99 (Paper No. 15), is acknowledged.
Claims 10, 11, 13, 14, 15, 18 and 19 have been amended.

Applicant's Petition to Review Restriction Requirement, filed 11/15/99, is acknowledged.
Given the administrative requirements to respond to applicant's Amendment (Paper No. 15); the Petition is held in abeyance with respect to this Office Action and will be responded to shortly. The examiner apologizes for any inconvenience to applicant in this matter.

The instant claims which have been amended to recite "a peptiodmimetic having the structure and function of human CD59 amino acid residues 42-58" as the active ingredient in the claimed methods.
Applicant's election with traverse of Group II and the species antibodies as defined by Claims 10-12 and 16-17 in Paper No. 11 has been acknowledged.
Since applicant has received an Office Action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits.
Therefore, the claimed methods still reads on methods of inhibiting C5-9 complex with antibodies that bind C9.
Claims 1-9, 13-15 and 18-35 have been withdrawn, as being drawn to the non-elected inventions and species, as set forth in the previous Office Action (Paper No. 12).

2. This Office Action will be in response to applicant's arguments, filed 11/15/99 (Paper No. 15)
The rejections of record can be found in the previous Office Action (Paper No. 12).

3. Claims 10-12 and 16-17 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention

There is insufficient direction or guidance provided to assist one skilled in the art in the selection of such "a peptiodmimetic having the structure and function of human CD59 amino acid residues 42-58" commensurate in scope with the claimed methods, nor is there sufficient evidence provided that all such "peptidomimetics " could be used in a practical manner either in vitro or in vivo to inhibit C5b-9 complex. The instant disclosure provides for certain C9-specific antibodies as well as certain CD59-derived constructs. Minor structural differences among structurally related compounds or compositions can result in substantially different pharmacological activities. Therefore, structurally unrelated compounds comprising antibodies, proteins, peptides, nucleic acids and small molecules would be expected to have greater differences in their activities, particularly when these diverse molecules are expected to have a particular three-dimensional structure that is suppose to mimic CD59. It would require undue experimentation to produce all such possible "molecules" without more explicit guidance from the disclosure. It would require undue experimentation to investigate all such "molecules". Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. It appears that undue experimentation would be required of one skilled in the art to practice the claimed "peptidomimetics" commensurate in scope with the claimed invention using the teaching of the specification.

Applicant's arguments, filed 11/15/99 (Paper No. 15), have been fully considered but are not found convincing essentially for the reasons of record and reiterated herein.

Applicant argues that the claims have been amended to refer to "peptidomimetics" having the structure and function of the region of the CD59 amino acids residues 42-58, as disclosed on page 11, lines 11-25 of the instant specification. Applicant also relies upon the computer modeling and screening assays disclosed in the specification.

However, as applicant acknowledges and the specification discloses; these peptidomimetics encompass a broad range of diverse and structurally distinct molecules. However, it appears that structural and/or functional requirements of such "peptidomimetics" is the ability of said "peptidomimetic" to inhibit C5b-9 complex formation.

In contrast to applicant's assertions and reliance upon the disclosure in the specification; the number of modifications such as single amino acid substitutions, that would be acceptable to retain the structural conformation and the inhibitory activity of amino acids residues 42-58 of SEQ ID NO: 3 are not well understood and are not predictable.

While the structural properties of said "peptidomimetics" should mimic or correspond to the three dimensional structure of amino acids residues 42-58 of SEQ ID NO: 3; neither the claims nor the specification is limited to such constraints nor clearly defines the structural constraints to said "peptidomimetics" . The physical conformation of said three dimensional structures rely upon the complex nature of primary, secondary and tertiary structures. The specification also discloses a number of modifications that would differ in the physical conformation that is limited three dimensional structure of amino acids residues 42-58 of SEQ ID NO: 3. Again, it appears the key constraint disclosed and claimed is a functional one (e.g. to inhibit C5b-9 complex formation) rather than a structural one (e.g. a particular amino acid sequence or type of molecule).

It is noted that the Examples disclosed in the specification indicate that varying structural modification impart varying functional properties.

Further, it appears that as the elected invention, C9-specific antibodies are simply those antibodies that bind C9 which inhibit the C5b-9 complex. There is insufficient evidence that such molecules comprise the structural elements of amino acids residues 42-58 of human CD59.

However, it is noted that for examination purposes; antibodies that bind C9 and inhibit the C5b-9 complex read on the claimed peptidomimetic.

It is not sufficient to define a specificity by its principal biological activity, i.e. a peptiodmimetic having the structure and function of human CD59 amino acid residues 42-58", which in itself is ill-define, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property or here, both structural and functional properties. Thus, applicant has not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed "peptidomimetics" in manner reasonably correlated with the scope of the claimed methods broadly including any number of "peptidomimetics".

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth.

Without sufficient guidance, the changes which can be made in the structure of any "peptidomimetic" and still provide or maintain sufficient or the claimed activity and structural conformation is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue

Applicant's arguments are not found persuasive.

Applicant is invited to limit the claims to clearly recite the structurally distinct antibodies, proteins, peptides, nucleic acids and small molecules and to recite the appropriate structural and functional language.

4. Claim 10-12 and 16-17 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 10-12 and 16-17 are indefinite in the recitation of "a peptiodmimetic having the structure and function of human CD59 amino acid residues 42-58" because the characteristics of these "peptidomimetics", including as it reads on anti-C9 antibodies, as the elected invention is ambiguous and confusing. This language is vague and indefinite since it encompasses a myriad of different "peptidomimetics" and it is not apparent from the disclosure which particular "peptidomimetics" are being referred to. Applicant has not provided sufficient biochemical information (e.g. molecular weight, amino acid composition, N-terminal sequence, etc.) that distinctly identifies the claimed "peptidomimetics " encompassed by the claimed invention. The recitation of "peptidomimetics " fails to distinctly claim what that molecule is made up of. Therefore, there is insufficient information and guidance for the metes and bounds of the claimed "peptidomimetics". Here, the claims do not even claim that the antibodies necessarily bind C9, which is the elected invention.

With respect to the elected invention of anti-C9 antibodies; it is not clear that the skilled artisan would indicate that an anti-C9 antibody that inhibits the formation of human C5b-9 complex acts as a "peptidomimetic having the structure and function of CD59" rather than an antibody that binds C9 and inhibits C5b-9 complex formation. The claimed limitations as it reads on the elected invention of an "anti-C9 antibody" as a "peptidomimetic" in this case appears to be confusing.

Again, applicant is invited to amend the claims accordingly, particularly with respect to the elected invention.

Applicant's arguments, filed 11/15/99 (Paper No. 15), have been fully considered but are not found convincing essentially for the reasons of record and reiterated herein.

Applicant argues that the claims have been amended to refer to "peptidomimetics" having the structure and function of the region of the CD59 amino acids residues 42-58, as disclosed on page 11, lines 11-25 of the instant specification.

However, as applicant acknowledges and the specification discloses; these peptidomimetics encompass a broad range of diverse and structurally distinct molecules and do not appear to be limited to any particular structure but rather appear to rely on the ability of the peptiodmimetic to inhibit C5b-9 complex formation".

While this "recitation" itself may have some notion of the activity of the "peptidomimetics";, there is nothing in the claims which distinctly claims the "peptidomimetics". Applicant should particularly point out and distinctly claim the structural and functional attributes of the claimed "peptidomimetics". Claiming biochemical molecules by the recitation of "a peptiodmimetic having the structure and function of the region of the CD59 amino acids residues 42-58" fails to distinctly claim what those "peptidomimetic" is made up of.

On one hand, there is insufficient evidence that such anti-CD9 antibodies comprise the structural elements of amino acids residues 42-58 of human CD59. However, it appears that as the elected invention, C9-specific antibodies are simply those antibodies that bind C9 which inhibit the C5b-9 complex. It is noted that for examination purposes; antibodies that bind C9 and inhibit the C5b-9 complex read on the claimed "peptidomimetic".

Here, even claim 12 does not recite that specificity of the antibody is "C9" (e.g., anti-C9 antibody) which is the elected invention.

The metes and bounds of the structural and functional attributes of the claimed "peptidomimetics" is unclear.

For examination purposes and given the variability of structures that can serve as "peptidomimetics" and the variations of said "peptidomimetics:; it appears that structural or functional requirements of such "peptidomimetics" is the ability of said "peptidomimetic" to inhibit C5b-9 complex formation.

Applicant's arguments are not found persuasive.

As pointed out above; applicant is invited to limit the claims to clearly recite the structurally distinct antibodies, proteins, peptides, nucleic acids and small molecules and to recite the appropriate structural and functional language.

The applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06

5. Claims 10-12 and 16-17 are rejected under 35 U.S.C. § 102(b) as anticipated by or, in the alternative, under 35 U.S.C. § 103(a) as obvious over Sims et al. (U.S. Patent No. 5,550,108) (see entire document) for the reasons of record set forth in Paper No. 12.

Applicant's arguments, filed 11/15/99 (Paper No. 15), have been fully considered but are not found convincing essentially for the reasons of record and reiterated herein.

Applicant argues that Sims et al. does not teach what region of CD59 imparts species-specificity. Also, applicant argues that merely because an antibody binds C9 does not mean that the antibody mimics the region of CD59 which is at issue.

However as pointed out previously and indicated above; for examination purposes, it appears that as the elected invention, C9-specific antibodies are simply those antibodies that bind C9 which inhibit the C5b-9 complex. It is noted that for examination purposes; antibodies that bind C9 and inhibit the C5b-9 complex read on the claimed "peptidomimetic".

Sims et al. teaches the use of anti-C9 antibodies to inhibit C5b-9 complex and that antibodies that bind C9 which inhibit C5b-9 complex formation would have the inherent properties of the claimed methods. Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the referenced methods of using C9-specific antibodies to inhibit C5b-9 complex formation and complement-mediated inflammation.

The burden is on the applicant to establish a patentable distinction between the claimed and referenced

methods.

Applicant has not provided sufficient objective evidence to distinguish the claimed and referenced methods which appear to employ the same C9-specific antibodies which inhibit C5b-9 complex formation and complement-mediated inflammation.

Also, see.Ex parte Novitski 26 USPQ 1389 (BPAI 1993).

Applicant's arguments are not found persuasive.

6. Claims 10-12 and 16-17 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Sims et al. (U.S. Patent No. 5,550,108) in view of Chang et al. (J. Biol. Chem., 1994; 1449) for the reasons of record set forth in Paper No. 12.

Applicant's arguments, filed 11/15/99 (Paper No. 15), have been fully considered but are not found convincing essentially for the reasons of record and reiterated herein.

Applicant argues that Sims et al. does not teach what region of CD59 imparts species-specificity. Also, applicant argues that merely because an antibody binds C9 does not mean that the antibody mimics the region of CD59 which is at issue.

Also, applicant argues that Chang identifies the region of human C9 which is bound by human CD59, not the portion of CD59 which binds and asserts that one cannot extrapolate from the information relating to human C9 to obtain information about human CD59.

However as pointed out previously and indicated above; for examination purposes, it appears that as the elected invention, C9-specific antibodies are simply those antibodies that bind C9 which inhibit the C5b-9 complex. It is noted that for examination purposes; antibodies that bind C9 and inhibit the C5b-9 complex read on the claimed "peptidomimetic".

Sims et al. teaches the use of anti-C9 antibodies to inhibit C5b-9 complex and that antibodies that bind C9 which inhibit C5b-9 complex formation would have the expected properties of the claimed methods. The claimed functional limitations would be expected properties of the referenced methods of using C9-specific antibodies to inhibit C5b-9 complex formation and complement-mediated inflammation.

As pointed out previously, Chang et al. teaches the nature of the interaction between C9 and CD59, including identifying the peptide domain of human C9 that is bound by CD59 (e.g. residues 359-411) and the importance of these interactions in complement-mediated activities (see entire document).

Therefore, one of ordinary skill in the art at the time the invention was made would have been motivated to select for anti-C9 antibodies that inhibit C5b-9 complex formation in modulating complement-mediated inflammatory responses, including selecting for those anti-C9 antibodies that inhibit CD59-mediated interactions with C9 and the complement cascade. The residues of 359-384 of C9 would have been targeted given the screening for inhibiting C5b-9 complex formation and the role of these residues in CD59 binding, as taught by the references.

From the teachings of the references, it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

Applicant's arguments are not found persuasive.

7. No claim is allowed.

8. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Phillip Gambel, PhD.
Patent Examiner
Technology Center 1600
January 27, 2000

Phillip Gambel